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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/828,307 | 04/06/2001 | David Mack | | 7761 |

27194 7590 09/26/2003

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| EXAMINER |
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KIM, YOUNG J

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| ART UNIT | PAPER NUMBER |
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1637

DATE MAILED: 09/26/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/828,307

Applicant(s)

MACK ET AL.

Examiner

Young J. Kim

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 12-51 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 and 12-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 47-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

This Office Action responds the Amendment received on July 14, 2003 (Paper No. 14).

Preliminary Remark

This application contains claims withdrawn from further consideration, drawn to non-elected invention, non-elected with traverse in Paper No. 10. Applicants are requested to cancel the non-elected claims.

Claim Rejections - 35 USC § 112 - Maintained

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 47-51 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on January 14, 2003 is maintained for the reasons of record.

Applicants' arguments received on July 14, 2003 have been fully considered but they are not found persuasive.

Applicants argue that the claims now have been amended to become drawn to a method of detecting versus diagnosing, which does not require a "100% sensitivity or specificity."

This is not found persuasive because whether or not the method is drawn to a diagnosis or detection since the limitation stated in the phrase, "indicates that the first individual *has* breast or colorectal cancer," renders the claim that if there is a differential expression, then the individual *must have* cancer. Neither the evidence of record nor the prior art discloses a 100% disease diagnostic correlation via expression profiling.

Art Unit: 1637

Amending the claims to recite, "wherein the higher level of protein expression in the first breast or colorectal tissue sample indicates that the first individual *may have* breast or colorectal cancer," would overcome this rejection.

Claim Rejections - 35 USC § 102

The rejection of claims 47, 50, and 51 under 35 U.S.C. 102(e) as being anticipated by Penn et al. (US 2002/0048763 A1, published April 25, 2002, priority February 4, 2000), made in the Office Action mailed on January 14, 2003 is withdrawn in view of the Amendment received on July 14, 2003, amending the claims to remove the phrase, "fragment thereof."

Claim Rejections - 35 USC § 103

The rejection of claims 48 and 49 under 35 U.S.C. 103(a) as being unpatentable over Penn et al. (US 2002/0048763 A1, published April 25, 2002, priority February 4, 2000) in view of Keyomarsi et al. (U.S. Patent No. 5,543,291, issued August 6, 1996), made in the Office Action mailed on January 14, 2003 is withdrawn in view of the Amendment received on July 14, 2003, amending the claims to remove the phrase, "fragment thereof."

Double Patenting

The rejection of claim 50 under 35 U.S.C. 101 as claiming the same invention as that of claim 7 of copending Application No. 09/608,821, made in the Office Action mailed on January 14, 2003 is withdrawn in view of the Amendment received on July 14, 2003, filing a terminal disclaimer.

Art Unit: 1637

The Office acknowledges that the copending Application is now a U.S. Patent, No. 6,566,502, issued on May 20, 2003. The previous Office Action made a provision rejection because at the time of the rejection, the Application had not yet issued as a patent.

Claim Rejections - 35 USC § 112 – New Grounds

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation are summarized in *In Re Wands* (858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). They include (A) the quantity of experimentation necessary, (B) the amount of direction or guidance presented, (C) the presence or absence of working examples, (D) the nature of the invention, (E) the state of the prior art, (F) the relative skill of those in the art, (G) the predictability or unpredictability of the art, and (H) the breadth of the claims.

(A) Quantity of Experimentation: The quantity of experimentation is determined to be undue because it is an art recognized fact that there is not a 1:1 correlation between the level of mRNA and the level of its expressed protein. Therefore, absent evidence to the contrary, it would require undue experimentation in order to diagnose a breast cancer or colorectal cancer

Art Unit: 1637

based on a differential protein expression analysis when the specification only substantiates a diagnostic based on a differential nucleic acid (mRNA) expression analysis.

(B) Amount of Direction or guidance: The specification gives a well known, general description of a diagnostic based on protein assay without any specific disclosure as to whether the claimed protein was actually differentially expressed between the diseased and normal tissues.

(C) Absence of Working Example: Although the specification discloses that the mRNA encoding the claimed protein is differentially expressed (page 65, Example 2), there is *no* evidence that the claimed protein is differentially expressed.

(D) Nature of Invention: The nature of the invention relates to a disease diagnostics based on protein expression.

(E) State of prior art: Gygi et al. (Molecular and Cellular Biology, March 1999, Vol. 19, No. 3, pages 1720-1730) discloses the state of prior art in correlating protein expression level based on mRNA levels:

“We found that the correlation between mRNA and protein levels was *insufficient* to predict protein expression levels from quantitative mRNA data.” (Abstract).

(F) Skill level: The skill level of the artisan is considered to be high.

(G) Unpredictability of art: As demonstrated by Gygi et al., the art of correlating protein expression based on mRNA levels is *unpredictable*.

Although the specification gives the structure of (*i.e.*, the amino acid sequence) the protein and its predicted splice variant encoded by the differentially expressed mRNA, the specification would not reasonably guide a skilled practitioner to diagnose breast or colorectal

Art Unit: 1637

cancer based on the protein expression because the specification does not give any example in whether or not the claimed protein is differentially expressed between the diseased and normal tissues samples. The skilled practitioner would then be forced to look to the teachings/guidance of the prior art, the prior art of which would only the support the unpredictability in correlating protein expression based on only mRNA expression levels (per Gygi et al.).

Therefore, for the reasons set forth above, it would require undue experimentation to practice the invention as claimed.

Conclusion

No claims are allowed.


Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (703)-308-3905. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

9/23/03




KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

9/25/03